

Application No.: 09/471,669
Page 3

IN THE DRAWINGS:

Please replace drawing sheets 1-26 with drawing sheets 1-51.

REMARKS

Claims 1-48 and 51-113 are pending in the application. Claims 48 and 51-69 are currently under consideration, claims 49 and 50 having been canceled, and claims 1-47 and 70-113 having been withdrawn from consideration. Claims 63, 64, 67, and 68 have been amended. The amendments to claims 63, 64, 67, and 68 add no new matter to the application.

In response to the Notice of Draftsperson's Patent Drawing Review dated June 27, 2000, Applicants submit drawing sheets 1-51 to replace drawing sheets 1-26 as filed.

The Applicants note the objection to the specification and claims 51-66 made in the Office Action mailed October 22, 2001, paper No. 13 have been withdrawn. Applicants note the following rejections made in the Office Action mailed October 22, 2001, paper No. 13 have been withdrawn: the rejection of claims 62, 63, and 68 under 35 U.S.C. § 112, second paragraph; the rejection of claim 48 under 35 U.S.C. § 112, first paragraph; the rejection of claims 48 and 51-57 under 35 U.S.C. § 102; and, the rejection of claims 58-63 under 35 U.S.C. § 103(a).

Applicants believe that the cancellation of claim 50 moots the non-statutory double patenting rejection made in the Office Action mailed October 22, 2001, paper No. 13. OK

Objection to Claims 63, 67, and 68

Claims 63, 67, and 68 have been amended as suggested by the Examiner. Claim OK 63 has been amended to remove "[1-501]." Claim 67 has been amended to expand "APPwt" and "APPsw." Claim 68 has been amended to expand "APP." The amendments to claim 63 and ✓ OK claims 67-68 are wholly stylistic in nature.



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ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG
TGCTGCCTGCCACGGCACCCAGCACGGCATCCGGCTGCCCTGCG
CAGCGGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGA
GACCGACGAAGAGCCCCGAGGAGCCCCGGCCGGAGGGGCGAGCTTTGT
GGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGGCGAGGGCTACTAC
GTGGAGATGACCGTGGGCAGCCCCCGCAGACGCTCAACATCCTGG
TGGATACAGGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCACCC
CTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGG
ACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGA
AGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAAC
GTCATGTGCGTGCCAACATTGCTGCCATCACTGAATCAGACAAGTT
CTTCATCAACGGCTCCAACCTGGGAAGGCATCCTGGGGCTGGCCTATG
CTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCT
CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTG
TGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTG
GAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC
AGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTGAT
CATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCA
AGGAGTACAACTATGACAAGAGCATTGTGGACAGTGGCACCACCAAC
CTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCATCAAG
GCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGA
GCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCC
CAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTTCC
GCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTG
GCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATC
CACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTG
TCTTTGATCGGGCCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC
CATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTG
TCACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAGAT
GAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTGAGTGGCGCTGCC
TCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCC
CTGCTGAAG

FIG. 1A

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CCATGCCGGCCCCCTCACAGCCCCGCCGGGAGCCCCGAGCCCCGCTGCCCCAGG
CTGGCCGCGCGSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCT
GCTCCCGTGCTCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCCGGACCCG
GGGGCTGGCCCCAGGGCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCT
CCCTCTCCTGAGAAGCCACCAGCACCAACCAGACTTGGGGGCAGGCGCCA
GGGACGGACGTGGGCCAGTGCGAGCCCAGAGGGCCCCGAAGGCCGGGGCC
CACCATGGCCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG
TGCTGCCTGCCACGGCACCCAGCACGGCATCCGGCTGCCCTGCGCAGC
GGCTGGGGGGGCGCCCCCCTGGGGCTGCGGCTGCCCGGGGAGACCGACG
AAGAGCCCCGAGGAGCCCCGGCCGGAGGGGCAGCTTTGTGGAGATGGTGGAC
AACCTGAGGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGG
CAGCCCCCGCGACAGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTT
TGCAGTGGGTGCTGCCCCCACCCCTTCTGCTCGCTACTACCAGAGGCA
GCTGTCCAGCACATAACGGGACCTCCGGAAGGGTGTGTATGTGCCCTACAC
CCAGGGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGCATCCCC
ATGGCCCCAACGTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGA
CAAGTTCTTCATCAACGGCTCCAAGTGGGAAGGCATCCTGGGGCTGGCCTAT
GCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCTCTGG
TAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGG
CTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTGCGAGGGGAGCATGAT
CATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACC
ATCCGGCGGGAGTGATTATGAGGTGATCATTGTGCGGGTGGAGATCAAT
GGACAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATTG
TGGACAGTGGCACCACCAACCTTCGTTTGCCCCAAGAAAGTGTTTGAAGCTGC
AGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCTGATGGTTTC
TGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCAACCCTTGGAAC
ATTTTCCAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTT
CCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGC
CACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATCCACGGGC
ACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTTGATCGGG
CCCGAAAACGAATTGGCTTTGCTGTGACGCTTGCCATGTGCACGATGAGTT
CAGGACGGCAGCGGTGGAAGGCCCTTTGTACCTTGACATGGAAGACTG
TGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTAT
GTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGT
GTCAGTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTG
ATGACATCTCCCTGCTGAAGTGAGGAGGCCCATGGGCAGAAGATAGAGATT
CCCCTGGACCACACCTCCGTGGTTCACCTTGGTCAACAAGTAGGAGACACAGA
TGGCACCTGTGGCCAGAGCACCTCAGGACCCTCCCCACCCACCAATGCCT
CTGCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGGTTCCAGGGACTGTA
CCTGTAGGAAACAGAAAAGAGAAGAAAGAAGCACTCTGCTGGCGGGAATAC
TCTTGGTCACCTCAAATTTAAGTCGGGAAATTCTGCTGCTTGAACTTCAGCC
CTGAACCTTTGTCCACCATTCCTTTAAATTCTCCAACCCAAAGTATTCTTCTTT
TCTTAGTTTCAGAAAGTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCC
CTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGCCAAA
GTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGT
ATAAACAAGCCTAACATTGGTGCAAGATTGCCTCTTGAATT

FIG. 1B

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MAQALPWLLLWMGAGVLPAGHTQHGIRLPLRSGLGGA PLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRYRQLSSTYRDLRKG VY
VPYTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS
NWE GILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHS LYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKS IK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

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FIG. 2A

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ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQT
LNILVDTGSSNFAVGAAPHPFLHRYRQRQLSSTYRDLRKG VYVP
YTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLR LPPKKVFEEAAVKSIAA
SSTEKFPDGF WLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

FIG. 1	SUBCLASS
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FIG. 2B

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MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSG LGGAPLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVY
VPYTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS
NWEGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIAK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDEDYKDDDDK

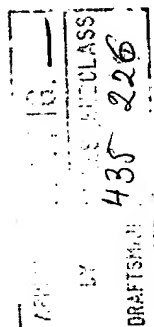
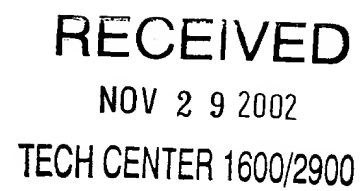


FIG. 3A

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVP
YTQGKWE GELGTDLV SIPHGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIAKAA
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDEDYKDDDDK

FIG. 3B

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Fig. 4



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Fig. 5A

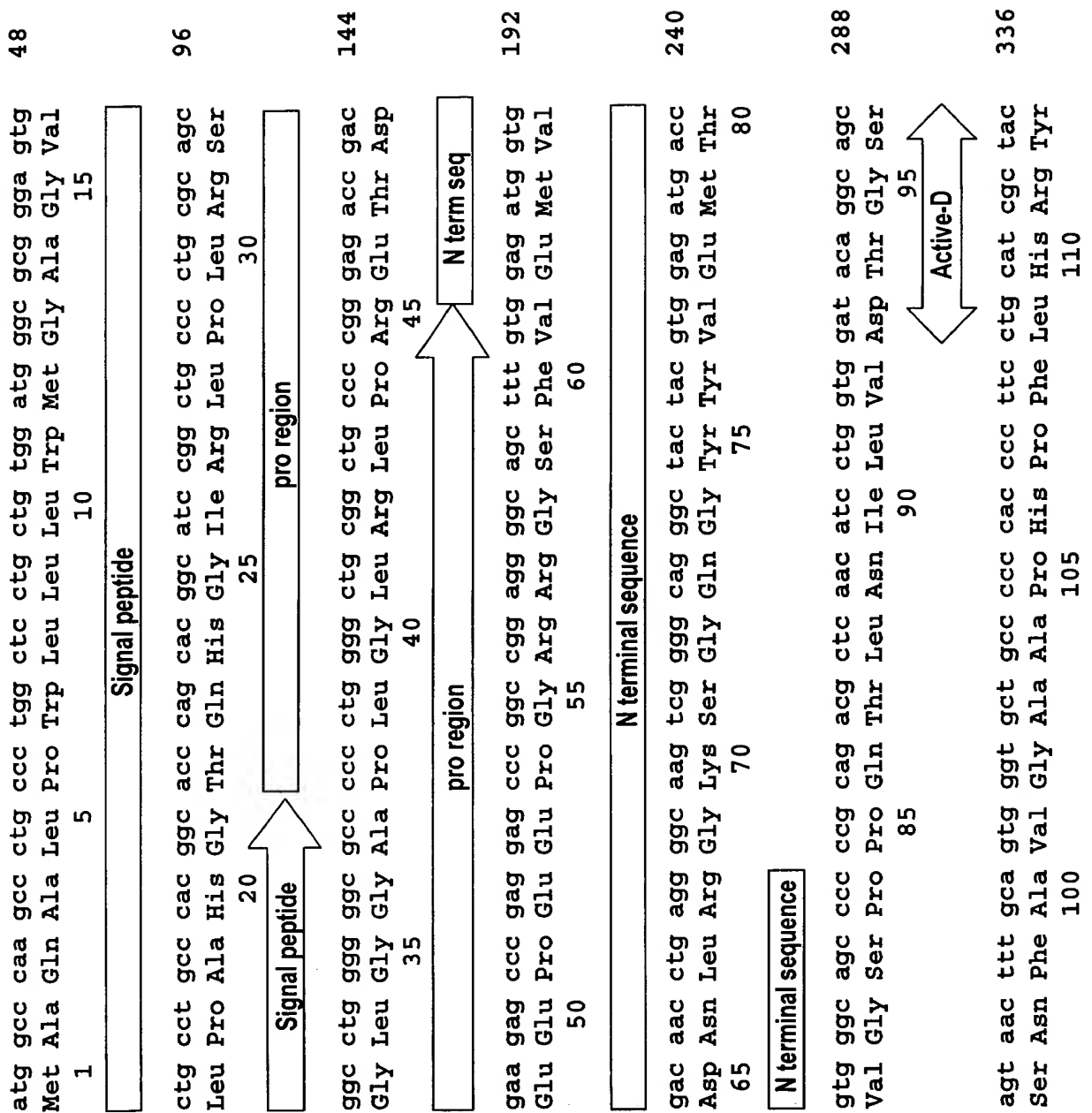




Fig. 5B

tac cag agg cag ctg tcc agc aca tac cgg gac ctc cgg aag ggt gtg 384
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
115 120 125

tat gtg ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac 432
Tyr Val Pro Tyr Thr Thr Gln Gly Lys Trp Glu Gly Thr Asp
130 135 140

ctg gta agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att 480
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
145 150 155 160

N-glycos

gct gcc atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg 528
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

N-glycos

gaa ggc atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac 576
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
180 185 190

tcc ctg gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc 624
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
195 200 205

aac ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag 672
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
210 215 220

N-glycos

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Fig. 5C

tct gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc 720
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
225 230 235 240

N-gly

gac cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg 768
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
245 250 255

gag tgg tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag 816
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260 265 270

gat ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg 864
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
275 280 285

gac agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct 912
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
290 295 300

Active-D

gca gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat 960
Ala Val Lys Ser Ile Lys Ala Ala Ser Thr Glu Lys Phe Pro Asp
305 310 315 320

ggt ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc 1008
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
325 330 335



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Fig. 5D

cct tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt 1056
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val 350
340 345

acc aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg 1104
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg 365
355 360

N-glycos

cca gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc 1152
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Cys Tyr Lys Phe Ala 380
370 375

atc tca cag tca tcc acg gcc act gtt atg gga gct gtt atc atg gag 1200
Ile Ser Gln Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu 400
385 390 395

ggc ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct 1248
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala 415
405 410

gtc agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa 1296
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 430
420 425

Internal peptide sequence

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1344

ggc cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
435 440 445

1392

cag aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
450 455 460

Transmembrane

1440

atc tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
465 470 475 480

Transmembrane

1488

cgc tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac
Arg Cys Leu Arg Cys Leu Arg Gln His Asp Asp Phe Ala Asp Asp
485 490 495

1506

atc tcc ctg ctg aag tga
Ile Ser Leu Leu Lys
500

Fig. 5E



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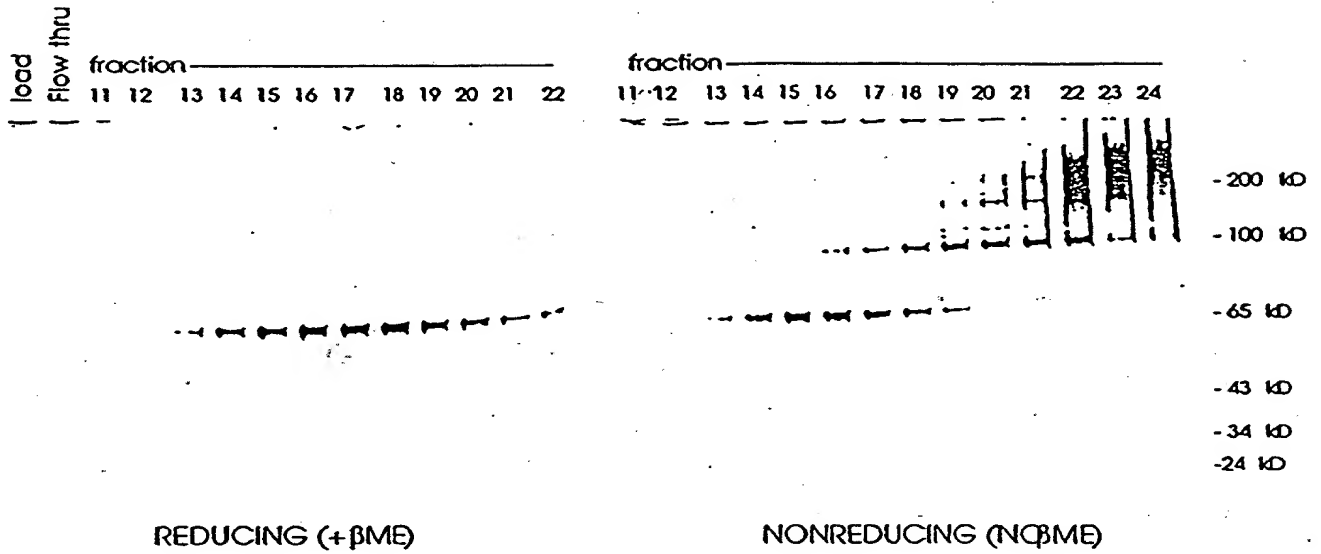


Fig. 6a

Fig. 6b

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Fig. 7

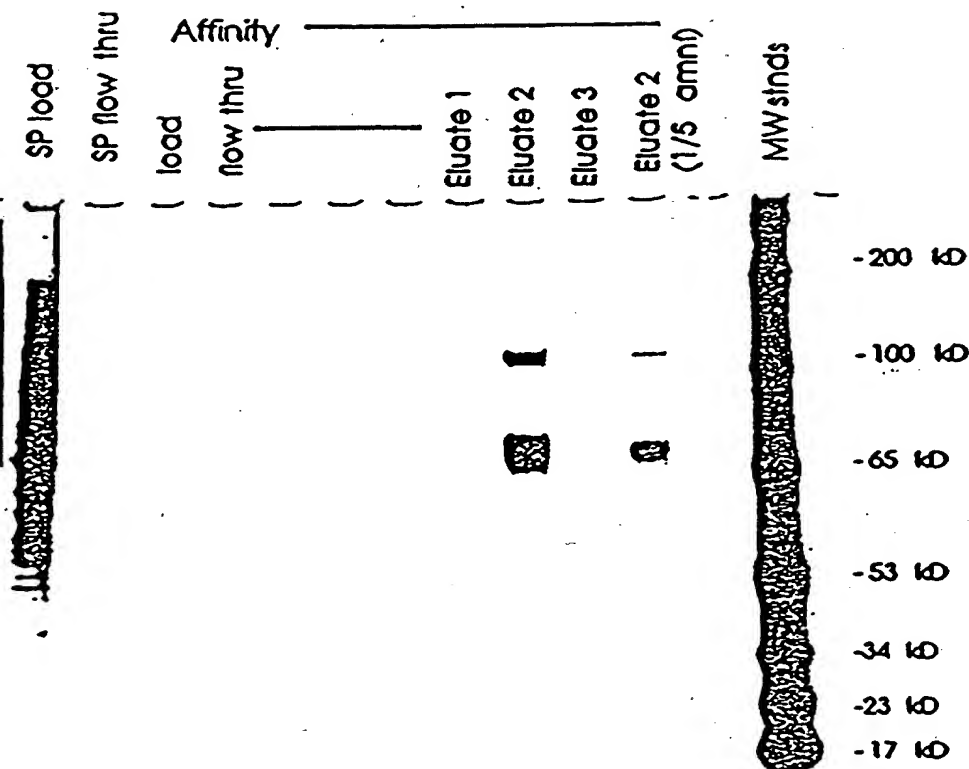
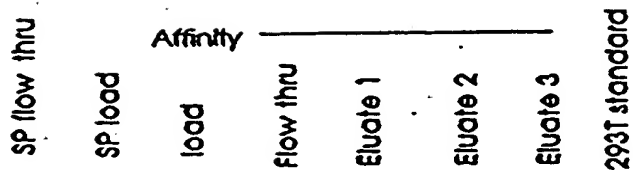


Fig. 8



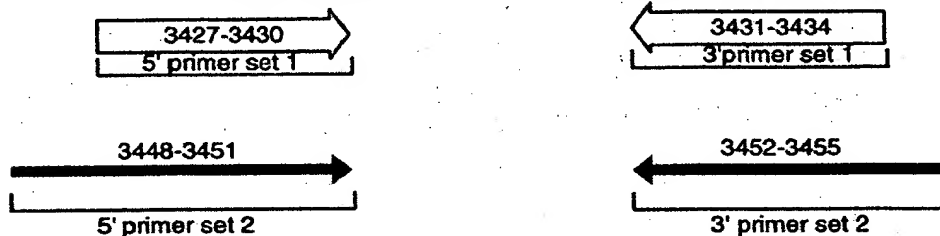


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E T D E E P E E P G R R G S F V E M V D N
GARACNGAYGARGARCCNGARGARCCNGGNMGMNGGGNWSNTTYGTNGARATGGTNGAYAAY 63



1° HNC/primer set 1

(3428+3433)
54 bp product

1° HNC & IMR32/ primer set 2

72 bp product

sequence:

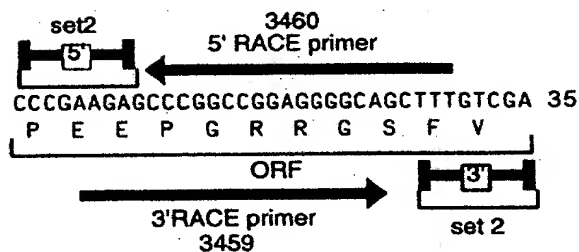


Fig. 9



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Human Impain Seq.	M A Q A L P W L L L W M G A G V L P A H G T Q H G I R L P L R S G
pBS/MuImpain E17 #11 cons	X X
pBS/MuImpain E17 #14 cons	- -
pBS/MuImpain E17 Brain#17cons	X X
pBS/MuImpain E17 Brain#15cons	- -
pBS/MuImpain H#3 cons	- -
Human Impain Seq.	L G G A P L G L R L P R E T D E E P G R R G S F V E M V D N
pBS/MuImpain E17 #11 cons	X X
pBS/MuImpain E17 #14 cons	- -
pBS/MuImpain E17 Brain#17cons	X X
pBS/MuImpain E17 Brain#15cons	- -
pBS/MuImpain H#3 cons	- -
Human Impain Seq.	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
pBS/MuImpain E17 #11 cons	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
pBS/MuImpain E17 #14 cons	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
pBS/MuImpain E17 Brain#17cons	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
pBS/MuImpain E17 Brain#15cons	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
pBS/MuImpain H#3 cons	L R G K S G Q G Y Y V E M T V G S P P Q T L N I L V D T G S S N F
Human Impain Seq.	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y
pBS/MuImpain E17 #11 cons	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y
pBS/MuImpain E17 #14 cons	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y
pBS/MuImpain E17 Brain#17cons	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y
pBS/MuImpain E17 Brain#15cons	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y
pBS/MuImpain H#3 cons	A V G A A P H P F L H R Y Y Q R Q L S S T Y R D L R K G V Y V P Y

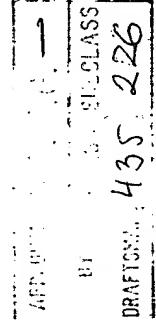
FIG. 10A



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Human Impain Seq.	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
pBS/MuImpPain E17 #11 cons	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
pBS/MuImpPain E17 #14 cons	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
pBS/MuImpPain E17 Brain#17cons	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
pBS/MuImpPain E17 Brain#15cons	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
pBS/MuImpPain H#3 cons	T	Q	G	K	W	E	G	E	L	G	T	D	L	V	S	I	P	H	G	P	N	V	T	V	R	A	N	I	A	A	I	T	E
Human Impain Seq.	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
pBS/MuImpPain E17 #11 cons	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
pBS/MuImpPain E17 #14 cons	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
pBS/MuImpPain E17 Brain#17cons	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
pBS/MuImpPain E17 Brain#15cons	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
pBS/MuImpPain H#3 cons	S	D	K	F	F	I	N	G	S	N	W	E	G	I	L	G	L	A	Y	A	E	I	A	R	P	D	D	S	L	E	P	F	F
Human Impain Seq.	D	S	L	V	K	Q	T	H	V	P	N	L	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	S	E	V	L	A	S	V
pBS/MuImpPain E17 #11 cons	D	S	L	V	K	Q	T	H	I	P	N	I	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	T	E	A	L	A	S	V
pBS/MuImpPain E17 #14 cons	D	S	L	V	K	Q	T	H	I	P	N	I	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	T	E	A	L	A	S	V
pBS/MuImpPain E17 Brain#17cons	D	S	L	V	K	Q	T	H	I	P	N	I	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	T	E	A	L	A	S	V
pBS/MuImpPain E17 Brain#15cons	D	S	L	V	K	Q	T	H	I	P	N	I	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	T	E	A	L	A	S	V
pBS/MuImpPain H#3 cons	D	S	L	V	K	Q	T	H	I	P	N	I	F	S	L	Q	L	C	G	A	G	F	P	L	N	Q	T	E	A	L	A	S	V
Human Impain Seq.	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I
pBS/MuImpPain E17 #11 cons	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I
pBS/MuImpPain E17 #14 cons	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I
pBS/MuImpPain E17 Brain#17cons	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I
pBS/MuImpPain E17 Brain#15cons	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I
pBS/MuImpPain H#3 cons	G	G	S	M	I	I	G	G	I	D	H	S	L	Y	T	G	S	L	W	Y	T	P	I	R	R	E	W	Y	Y	E	V	I	I

FIG. 10B



Human Impain Seq.		Q Q Y L R P V E D V A T S Q Q D D C Y K F A I S Q S S T G T V M G A
pBS/MuImpPain E17 #11 cons		Q Q Y L R P V E D V A T S Q Q D D C Y K F A V S Q S S T G T V M G A
pBS/MuImpPain E17 #14 cons		Q Q Y L R P V E D V A T S Q Q D D C Y K F A V S Q S S T G T V M G A
pBS/MuImpPain E17 Brain#17cons		Q Q Y L R P V E D V A T S Q Q D D C Y K F A V S Q S S T G T V M G A
pBS/MuImpPain E17 Brain#15cons		Q Q Y L R P V E D V A T S Q Q D D C Y K F A V S Q S S T G T V M G A
pBS/MuImpPain H#3 cons		Q Q Y L R P V E D V A T S Q Q D D C Y K F A V S Q S S T G T V M G A



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Human Impain Seq.	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
pBS/MuImpain E17 #11 cons	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
pBS/MuImpain E17 #14 cons	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
pBS/MuImpain E17 Brain#17cons	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
pBS/MuImpain E17 Brain#15cons	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
pBS/MuImpain H#3 cons	V I M E G F Y V V F D R A R K R I G F A V S A C H V H D E F R T A
Human Impain Seq.	A V E G P F V T L D M E D C G Y N I P Q T D E S T L M T I A Y V M
pBS/MuImpain E17 #11 cons	A V E G P F V T A D M E D C G Y N N R I P A A R G I
pBS/MuImpain E17 #14 cons	A V E G P F V T A D M E D C G Y N N R I Q
pBS/MuImpain E17 Brain#17cons	A V E G P F V T A D
pBS/MuImpain E17 Brain#15cons	A V E G P F V T A D M E D G Y N N R I P A A R G I H F S G R
pBS/MuImpain H#3 cons	A A I C A L F M L P L C L M V C Q W R C L R C L R Q Q H D D F A D
Human Impain Seq.	H R G G A P I R P I V S R I N
pBS/MuImpain E17 #11 cons	D I S L L K
pBS/MuImpain E17 #14 cons	
pBS/MuImpain E17 Brain#17cons	
pBS/MuImpain E17 Brain#15cons	
pBS/MuImpain H#3 cons	
Human Impain Seq.	
pBS/MuImpain E17 #11 cons	
pBS/MuImpain E17 #14 cons	
pBS/MuImpain E17 Brain#17cons	
pBS/MuImpain E17 Brain#15cons	
pBS/MuImpain H#3 cons	

FIG. 10D



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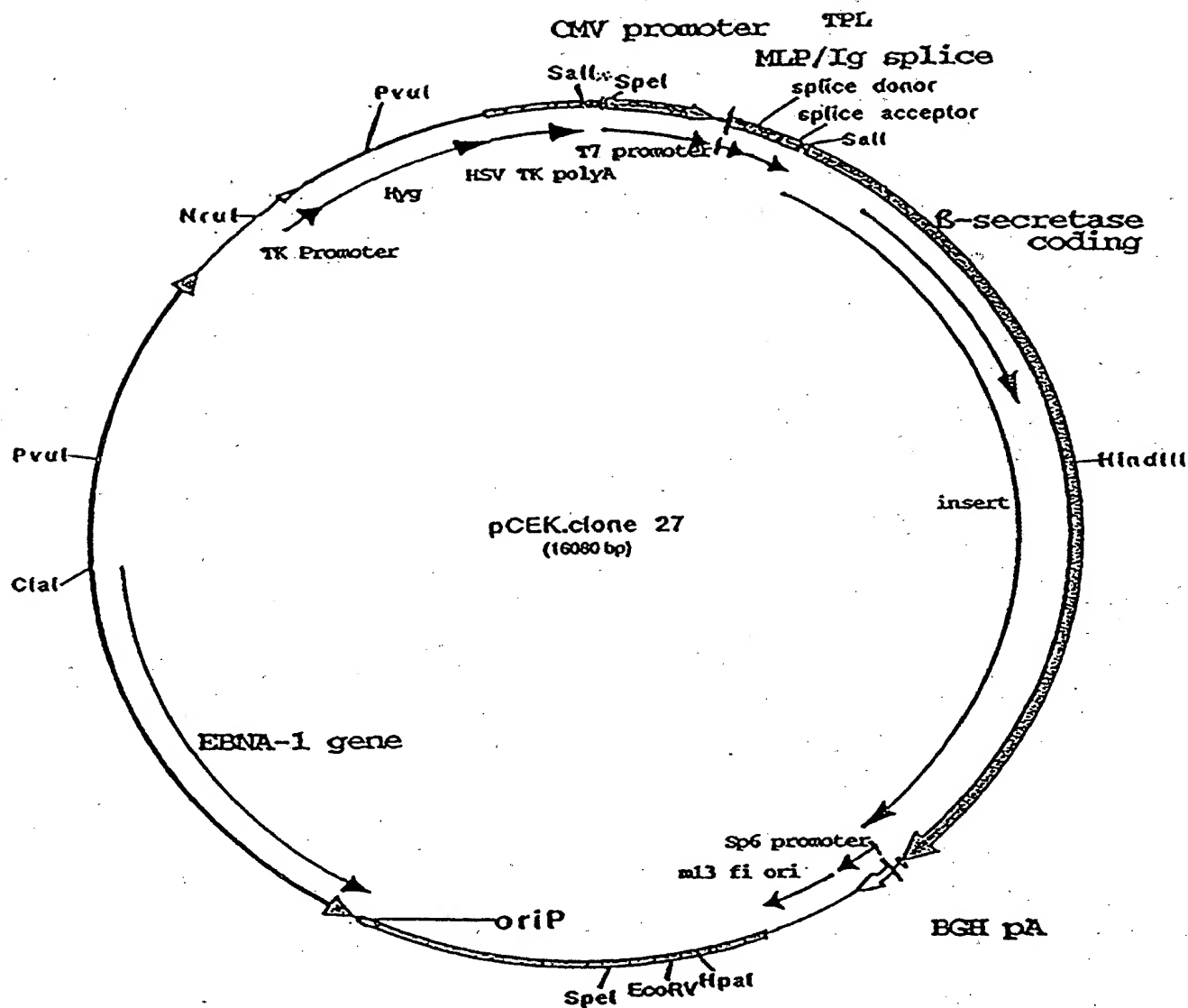


Fig. 12

FIG. 12
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Figure 13A

ttctcatggt tgacagctta tcatcgcaga tccgggcaac gttgttgcat tgctgcaggc 60
gcagaaactgg taggtatgga agatccgatg tacgggccag atatacgcgt tgacattgat 120
tattgactag ttattaatag taatcaatta cgggggtcatt agttcatagc ccatatatgg 180
agtccgcgt tacataactt acggtaaatg gccgcctgg ctgaccgcc aacgaccccc 240
gccattgac gtcaataatg acgtatgttc ccatagtaac gccaataggg actttccatt 300
gacgtcaatg ggtggactat ttacggtaaa ctgccactt ggcagtacat caagtgtatc 360
atatgccaaag tacgccccct attgacgtca atgacggtaa atggccgcc tggcattatg 420
cccagtacat gaccttatgg gactttccta cttggcagta catctacgta ttagtcatcg 480
ctattaccat ggtgatcgg ttttggcagt acatcaatgg gcgtggatag cggtttgact 540
cacggggatt tccaagtctc caccattg acgtcaatgg gagtttgttt tggcaccaaa 600
atcaacggga ctttccaaa tgctgtaaca actccgccc attgacgcaa atggcggtgta 660
ggcgtgtacg gtgggaggtc tataaagca gagctctctg gctaactaga gaaccactg 720
cttactggct tatcgaaatt aatacactc actatagga gacccaagct ctgttgggct 780
↑
↑



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Figure 13B

cgcggttgag gacaaactct tcgcggtctt tccagtactc ttggatcgga aaccggtcgg 840
cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac cggatcggaa 900
splice donor
aacctctcga ctgttgggggt gagtactccc tctcaaaagc gggcatgact tctgcgctaa 960
gattgtcagt ttccaaaaac gaggaggatt tgatatcac ctggcccgcg gtgatgcctt 1020
tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca agcttgaggt 1080
gtggcaggct tgagatctgg ccatacactt gagtgacaat gacatccact ttgcctttct 1140
splice acceptor splice acceptor
ctccacaggt gtccactccc aggtccaact gcaggctcgac tctagaccgc ggaattctg 1200
cagatatcca tcacactggc cgcactctgc ccagcccgc cgggagctg cgagccgcga 1260
gctggattat ggtggcctga gcagccaacg cagccgcagg agccggagc cctggccct 1320
gcccgcgcg ccgcccgcg gggggaccag ggaagccgcc accggcccgc catgcccgcc 1380
cctcccagcc ccgccgggag cccgcgcccgc ctgcccaggc tggccgcccgc cgtgccgatg 1440
tagcgggctc cggatcccag cctctcccct gctcccgtgc tctgaggatc tcccctgacc 1500
gctctccaca gcccgacc gccggctggc ccagggccct gcaggccctg gcgtcctgat 1560
gcccccaagc tccctctctt gagaagccac cagcaccacc cagacttggg ggcaggcgcc 1620

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Figure 13C

1677	aggacggac gtgggccagt gcagcccag agggcccgaa ggccggggcc cacc atg	Met
		<u>1</u>
1725	gcc caa gcc ctg ccc tgg ctc ctg ctg tgg atg ggc gcg gga gtg ctg	
	Ala Gln Ala Leu Pro Trp Leu Leu Trp Met Gly Ala Gly Val Leu	
	5 10 15	
1773	cct gcc cac gcc acc cag cac gcc atc cgg ctg ccc ctg cgc agc ggc	
	Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly	
	20 25 30	
1821	ctg ggg ggc gcc ccc ctg ggg ctg cgg ctg ccc cgg gag acc gac gaa	
	Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu	
	35 40 45	
1869	gag ccc gag gag ccc ggc cgg agg ggc agc ttt gtg gag atg gtg gac	
	Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp	
	50 55 60 65	
1917	aac ctg agg ggc aag tcg ggg cag ggc tac gtg gag atg acc gtg	
	Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val	
	70 75 80	
1965	ggc agc ccc ccg cag acg ctc aac atc ctg gtg gat aca ggc agc agt	
	Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser	
	85 90 95	



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Figure 13D

2013	aac ttt gca gtg ggt gct gcc ccc cac ccc ccc ccc cat ctg ctg cat cgc tac tac	110	Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr	105
2061	cag agg cag ctg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat	115	Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr	120
2109	gtg ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg	130	Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Thr Asp Leu	135
2157	gta agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att gct	150	Val Ser Ile Pro His Gly Pro Asn Val Thr Arg Ala Asn Ile Ala	155
2205	gcc atc act gaa tca gac aag ttc atc aac ggc tcc aac tgg gaa	165	Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu	170
2253	ggc atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc	180	Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser	185
2301	ctg gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac	195	Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn	200



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Figure 13E

ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct	2349
Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser	
210 215 220 225	
<hr/>	
gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac	2397
Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp	
230 235 240	
<hr/>	
cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg gag	2445
His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu	
245 250 255	
<hr/>	
tgg tat tat gag gtc atc att gtg cgg gtg gag atc aat gga cag gat	2493
Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp	
260 265 270	
<hr/>	
ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac	2541
Leu Lys Met Asp Cys Lys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp	
275 280 285	
<hr/>	
agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca	2589
Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala	
290 295 300 305	
<hr/>	
gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat ggt	2637
Val Lys Ser Ile Lys Ala Ala Ser Thr Glu Lys Phe Pro Asp Gly	
310 315 320	

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Figure 13F

ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro 325 330 335	2685
tgg aac att ttc cca gtc atc tca ctc tac atg ggt gag gtt acc Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr 340 345 350	2733
aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg cca Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro 355 360 365	2781
gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile 370 375 380 385	2829
tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag ggc Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly 390 395 400	2877
ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val 405 410 415	2925
agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly 420 425 430	2973

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Figure 13G

cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca cag	3021
Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln	
435 440 445	
aca gat gag tca acc ctg atg acc ata gcc tat gtc atg gct gcc atc	3069
Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile	
450 455 460 465	
tgc gcc ctg ttc atg ctg cca ctg tgc ctg atg gtg tgt cag tgg cgc	3117
Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg	
470 475 480	
tgc ctg cgc tgc ctg cgc cag cat gat gac ttt gct gat gac atc	3165
Cys Leu Arg Cys Leu Arg Gln Gln His Asp Phe Ala Asp Asp Ile	
485 490 495	
tcc ctg ctg aag tga ggaggcccat gggcagaaga tagagattcc cctggaccac	3220
Ser Leu Leu Lys	
500	
acctccgtgg ttcaacttgg tcacaagtag gagacacaga tggcacctgt ggcagagca	3280
cctcaggacc ctcccaccc accaaatgcc tctgccttga tggagaagga aaaggctggc	3340
aaggtagggtt ccagggactg tacctgtagg aaacagaaaa gagaagaaag aagcactctg	3400
ctggcgggaa tactcttggt cacctcaaat ttaagtcggg aaattctgct gcttgaaact	3460



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Figure 13H

tcagccctga acctttgtcc accattcctt taaattctcc aacccttctt attcttcttt 3520

tcttagtttc agaagtactg gcatcacacg caggttacct tggcgtgtgt ccctgtggta 3580

HindIII

ccctggcaga gaagagacca agcttgtttc cctgctggcc aaagtcagta ggagaggatg 3640

cacagttgc tatttgcttt agagacaggg actgtataaa caagcctaac attggtgcaa 3700

agattgcctc ttgaattaaa aaaaaaact agattgacta ttatacaaa tggggggcggc 3760

tggaaagagg agaaggagag ggagtacaaa gacaggggaat agtgggatca aagctaggaa 3820

aggcagaaac acaaccactc accagtccta gttttagacc tcactctcaa gatagcatcc 3880

catctcagaa gatgggtgtt gttttcaatg ttttcttttc tgtggttgca gcctgaccaa 3940

aagtgatg ggaagggtt atctagccaa agagctcttt ttagctctc ttaaatgaag 4000

tgcccactaa gaagtccac ttaacacatg aatttctgcc atattaattt cattgtctct 4060

atctgaacca ccctttattc tacatatgat aggcagcact gaaatatcct aacccctaa 4120

gctccagggt ccctgtggga gagcaactgg actatagcag ggctgggctc tgtcttctctg 4180

gtcataggct cactcttcc cccaaatctt cctctggagc ttgcagcca aggtgctaaa 4240

aggaatagggt aggagacctc ttctatctaa tccttaaaag cataatgttg aacattcatt 4300

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Figure 13I

caacagctga tgcctataa cccctgcctg gatttcttcc tattaggcta taagaagtag 4360
caagatcttt acataattca gagtgggttc attgccttcc taccctctct aatggccccc 4420
ccatttatatt gactaaagca tcacacagtg gcactagcat tataccaaga gtatgagaaa 4480
tacagtgcct tatgggtcta acattactgc cttcagtatc aaggctgcct ggagaaaagga 4540
tggcagcctc agggcttcct tatgtcctcc accacaagag ctcttgatg aaggtcatct 4600
ttttccccta tcctgttctt cccctccccg ctccaatgg tacgtgggtg cccaggctgg 4660
ttcttgggct aggtagtggg gaccaagttc attacctccc tatcagttct agcatagtaa 4720
actacggtac cagtgttagt gggaagagct gggttttcct agtatacca ctgcctccta 4780
ctcctacctg gtcaaccgc tgctccagg tatgggacct gctaagtgtg gaattacctg 4840
ataagggaga gggaaatata aggagggcct ctggtgttcc tggcctcagc cagctgcccc 4900
caagccataa accaataaaa caagaatact gagtcagttt ttatctggg ttctcttcat 4960
tcccactgca cttgggtgctg ctttggctga ctgggaacac ccataacta cagagtctga 5020
caggaagact ggagactgtc cactcttagc tcggaactta ctgtgtaaat aaactttcag 5080
aactgctacc atgaagtga aatgccacat ttgcttttat aatttctacc catgttggga 5140

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Figure 13J

aaaactggct tttcccagg cttttccagg gcataaaact caacccttc gatagcaagt 5200

cccatcagcc tattatttt ttaaagaaaa cttgcacttg tttttctttt tacagttact 5260

tccttcctgc cccaaaaatta taaactctaa gtgtataaaaa aagtcttaac aacagcttct 5320

tgcttgtaaa aatatgtatt atacatctgt atttttaaat tctgctcctg aaaaatgact 5380

gtcccattct cactcactg catttggggc ctttccatt ggtctgcatg tcttttatca 5440

ttgcaggcca gtggacagag ggagaaggga gaacaggggt cgccaacact tgtgttgctt 5500

tctgactgat cctgaacaag aaagagtaac actgaggcgc tcgctcccat gcacaactct 5560

ccaaaacact tatcctcctg caagagtggg ctttccgggt ctttactggg aagcagttaa 5620

gccccctct cacccttcc tttttcttt ctttactcct ttggcttcaa aggattttgg 5680

aaaagaaaca atatgcttta cactcathtt caatttctaa atttgcaggg gatactgaaa 5740

aatacggcag gtggcctaag gctgctgtaa agttgagggg agaggaaatc ttaagattac 5800

aagataaaaa acgaatcccc taaacaaaaa gaacaataga actggtcttc cattttgcc 5860

cctttcctgt tcatgacagc tactaacctg gagacagtaa catttcatta accaaagaaa 5920

gtgggtcacc tgacctctga agagctgagt actcaggcca ctccaatcac cctacaagat 5980

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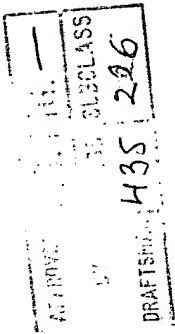


Figure 13K

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aaagacggaa aagagtatca aaggcagaaa ggagatcatt tagttgggtc tgaaaggaaa 6160
agntttgct atccgacatg tactgctagt wctgtaagc atttaggtc ccagaatgga 6220
aaaaaaaaa aagctatngg ttatataata atgnnnnnnn nntcgagcat 6280
gcatctagag ggcctattc tatagtgtca cctaaatgct agagctcgct gatcagcctc 6340
gactgtgcct tctagttgcc agccatctgt tgtttgcccc tcccccgctc cttccttgac 6400
cctggaagggt gccactccca ctgtccttct ctaataaaat gaggaaatg catcgcatg 6460
tctgagtagg tgtcattcta ttctgggggg tggggtgggg caggacagca agggggagga 6520
ttgggaagac aatagcaggc atgctgggga tgcggtgggc tctatggctt ctgaggcgga 6580
aagaaccagc tggggctcta gggggtatcc ccacgcgccc tgtagcggcg cattaagcgc 6640
ggcgggtgtg gtggttacgc gcagcgtgac cgctacactt gccagcgccc tagcgccccg 6700
tcctttcgct ttcttccctt cctttctcgc cacttcgcc ggctttcccc gtcaagctct 6760
aaatcggggc atcccttttag ggttccgatt tagtgcttta cggcacctcg acccaaaaa 6820

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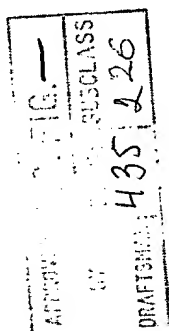


Figure 13L

acttgattag ggtgatggtt cacgtagtgg gccatcgccc tgatagacgg tttttcgccc 6880
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caaccctatc tcggtctatt cttttgattt ataagggatt ttggggattt cggcctattg 7000
gttaaaaaat gagctgattt aacaaaaaatt taacgcgaat tctagagccc cgccgccgga 7060
cgaactaaac ctgactacgg catctctgcc ccttcttcgc ggggcagtgc atgtaatccc 7120
ttcagttggt tggtaacaact tgccaactgg gccctgttcc acatgtgaca cgggggggga 7180
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cattgccttt atgtgtaact cttggctgaa gctcttacac caatgctggg ggacatgtac 7360
ctcccagggg cccaggaaga ctacgggagg ctacaccaac gtcaatcaga ggggcctgtg 7420
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HpaI
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EcoRV
aaagggctct aaggaacagc gatattctcc accccatgag ctgtcacgggt tttatttaca 7660

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Figure 13M

tggggtcagg attccacgag ggtagtgaaac cattttagtc acaaggggcag tggctgaaga 7720

tcaaggagcg ggcagtgaac tctcctgaat cttcgcctgc ttcttcattc tccttcgttt 7780

agctaataga ataactgctg agttgtgaac agtaagggtg atgtgaggtg ctcgaaaaa 7840

aggtttcagg tgacgcccc agaataaaat ttggacgggg ggttcagtggtg tggcattgtg 7900

ctatgacacc aatataaacc tcacaaaacc cttgggcaat aaatactagt gtaggaatga 7960

SpeI

aacattctga atatctttaa caatagaaat ccatggggtg gggacaaagcc gtaaagactg 8020

gatgtccatc tcacacgaat ttatgggctat gggcaacaca taatccctagt gcaatatgat 8080

actgggggta ttaagatgtg tccaggcag ggaccaagac aggtgaacca tgttgttaca 8140

ctctatttgt aacaaggga aagagagtgg acgccgacag cagcggactc cactggttgt 8200

ctctaacacc ccgaaaaat aaacggggct ccacgccaat gggggccata aacaaaagaca 8260

agtggccact ctttttttg aaattgtgga gtgggggcac gcgtcagccc ccacacgccg 8320

ccctgcgggtt ttggactgta aaataagggt gtaataactt ggctgattgt aaccccgcta 8380

accactgcgg tcaaaaccact tgcccacaaa accactaatg gcaccccggtg gaataacctg 8440

ataagtaggt gggcggggcca agataggggc gcgattgctg cgatctggag gacaaattac 8500



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Figure 13N

acacacttgc gcctgagcgc caagcacagg gttgttggtc ctcatattca cgaggctgct 8560
gagagcacgg tgggctaag ttgccatggg tagcatatac tacccaaata tctggatagc 8620
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gctatccctca tgcatacata gtcagcatat gataccagc agtagagtgg gagtgcctatc 9220
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catgctggtt gctcccatc ttaggtgaat ttaaggaggc caggctaaag ccgtcgcatg 9340
orip

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Figure 130

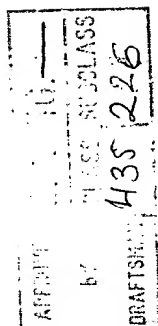
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acccaagttc cttcgtcgggt agtcctttct acgtgactcc tagccaggag agctcttaaa 10060
ccttctgcaa tgttctcaaa ttctgggttg gaacctcctt gaccacgatg ctttccaaac 10120
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Figure 13P

tctcctgggt catctgcggg gccctgctct atcgctccc ggggcacgtc aggtcaccca 10240

tctggggccac cttcttggtg gtattcaaaa taatcggtt cccctacagg gtggaaaaat 10300

ggcctttctac ctggaggggg cctgcgcggt ggagaccagg atgatgatga ctgactactg 10360

ggactcctgg gcctctttt tccacgtcca cgacctctcc cctgggtctt ttcacgactt 10420

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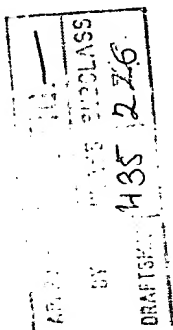
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gcccctcctg cccctcctcc tgctcctgcc cctcctcctg ctctgcccc tcttgcccc 11020





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Figure 13Q

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cctgcccc ctcctcctgc cctccccgt cctgtctctg ctcctgttcc accgtgggtc 11260
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ctcatcacca attactcgca gcccggaata ctcctgctga acatcctcaa gatttgcgtc 11740
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Figure 13R

Clai

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PvUI

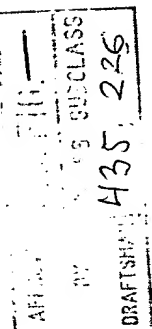


Figure 13S

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aggatctagg tgaagatcct ttttgataat ctcatgacca aaatccctta acgtgagttt 13120
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Figure 13T

agatacctac agcgtgagct atgagaaagc gccacgcttc ccgaagggag aaagcgggac 13600

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aatccatgcc aaccggttcc atgtgctcgc cgaggcggca taaatcgccg tgacgatcag 14080

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ggaagcgaga agaatacataa tggggaaggc catccagcct cgcgtcgcga acgccagcaa 14260

gacgtagccc agcgcgtcgg ccgccatgcc ctgcttcac cccgtggccc gttgctcgcg 14320

tttgctggcg gtgtcccccg aagaaatata tttgcattgc tttagttcta tgatgacaca 14380

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Figure 13U

aacccgcc agcgtcttgt cattggcgaa ttcgaacacg cagatgcagt cggggcggcg 14440
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ggaattcage gagagcctga cctattgcat ctccgccgt gcacaggggtg tcacgttgca 14860
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Figure 13V

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cgggcgtctg tggctgcaa acacccccga cccccaaa ccaccgcgcg gatttctggc 16060

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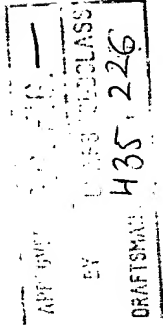


Figure 13W

Sali

gtgccaaagct agtcgaccaa





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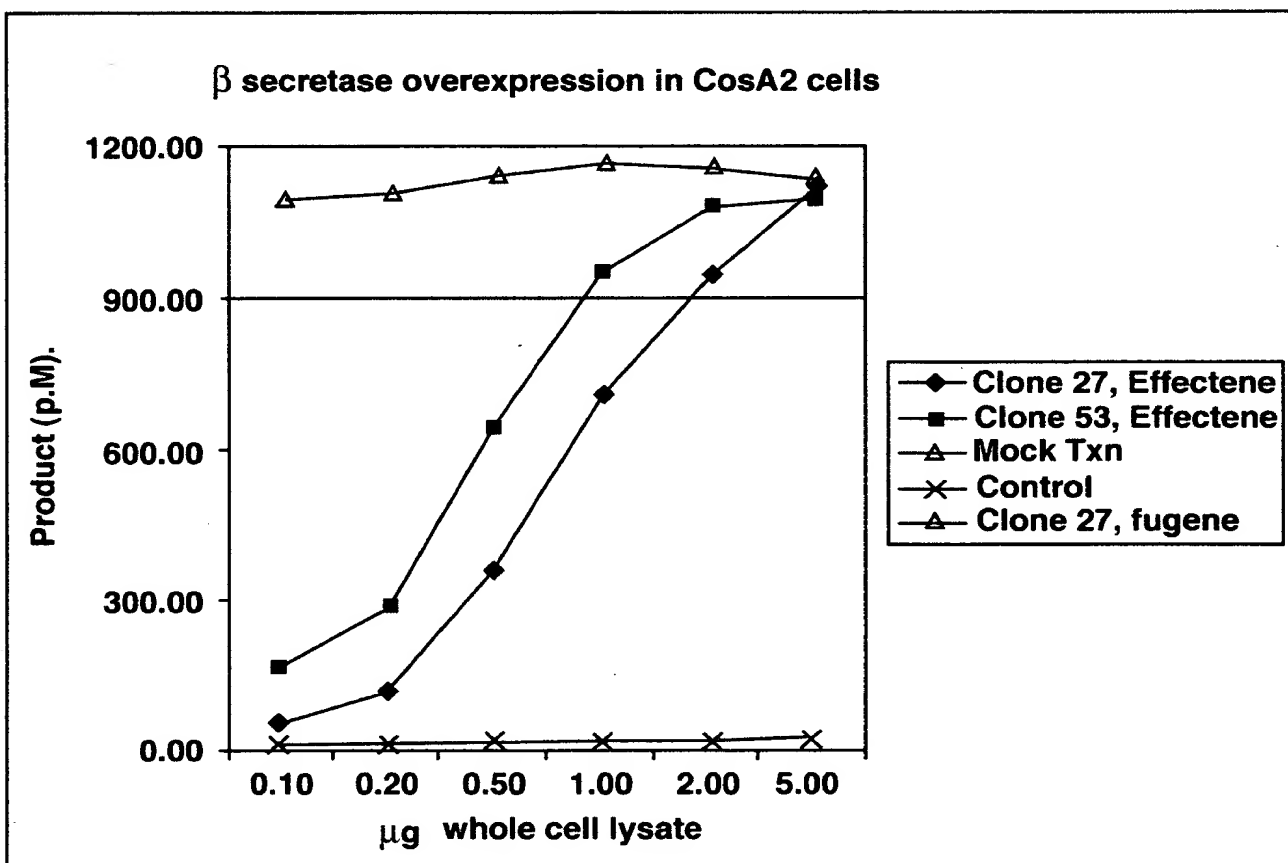


Fig. 14



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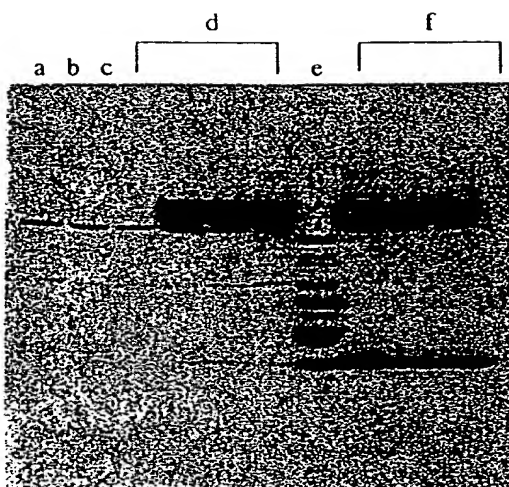


FIG. 15A

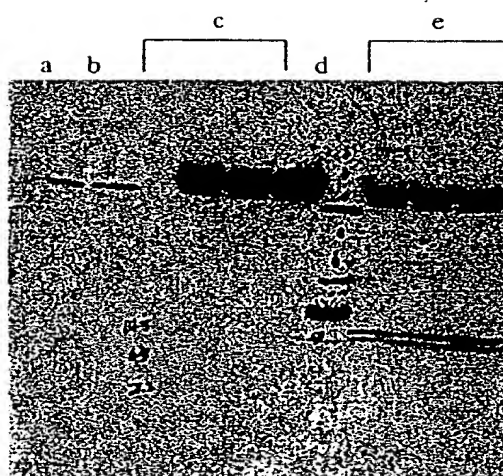
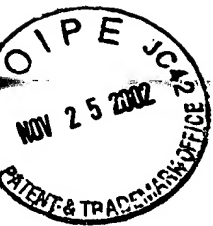


FIG. 15B



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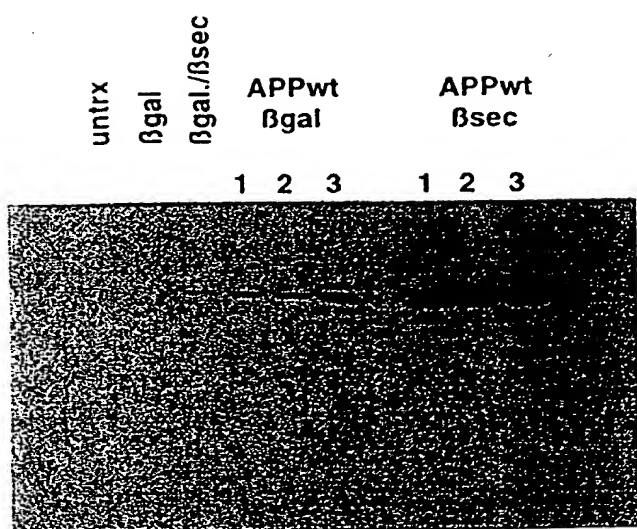


FIG. 16A

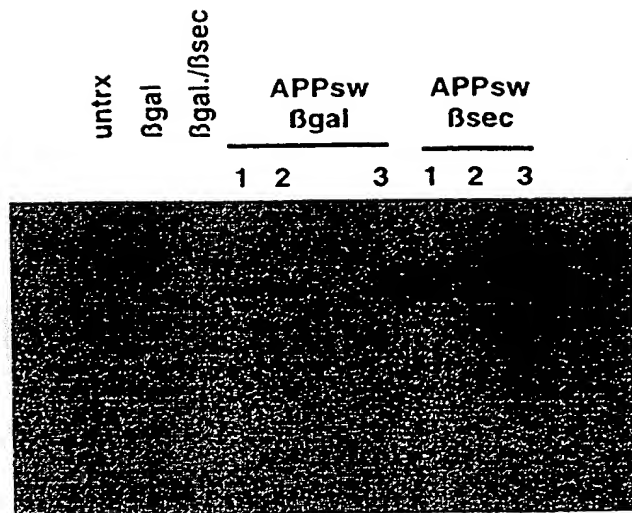


FIG. 16B



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β gal	APPwt β gal			APPwt β sec		
	1	2	3	1	2	3



FIG. 17A

β gal	APPsw β gal			APPsw β sec		
	1	2	3	1	2	3



FIG. 17B



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10	435	226	
DRAFTSMAN			

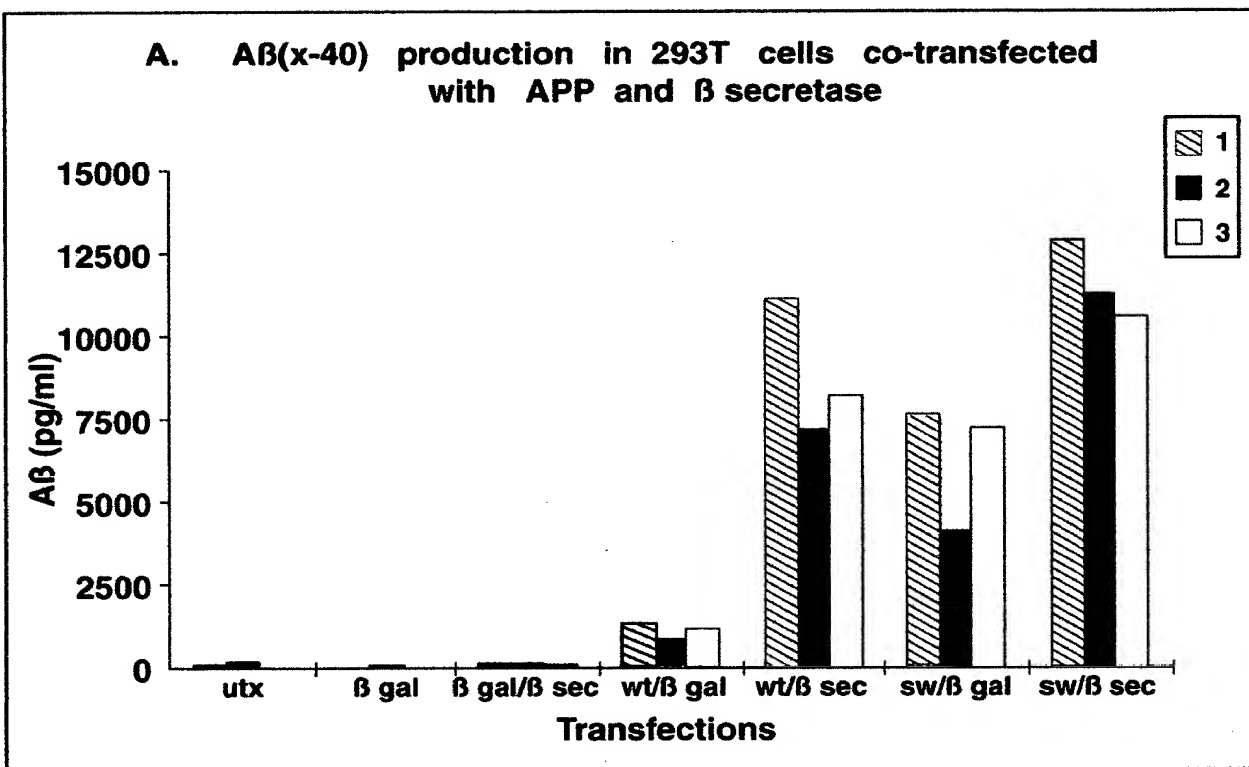
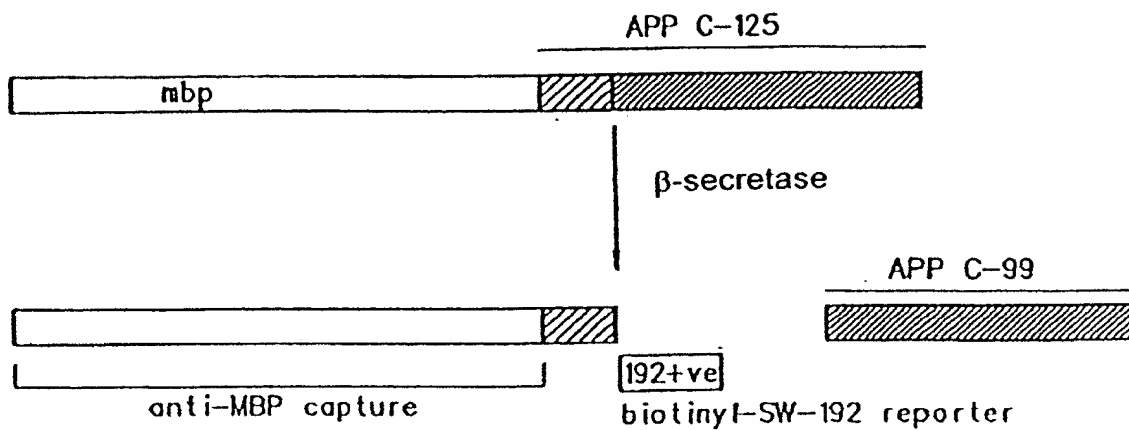


Fig. 18



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Wild-Type SequenceVal-Lys-Met-Asp...
Swedish SequenceVal-Asn-Leu-Asp...

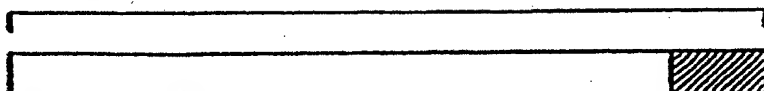
Fig. 19



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APP 638



β -secretase

8E5



A β



192+ve

Detected by: 1. SW192 Western Blot
2. 8E5-192 ELISA

Wild-Type SequenceVal-Lys-Met-Asp...
Swedish SequenceVal-Asn-Leu-Asp...

Fig. 20



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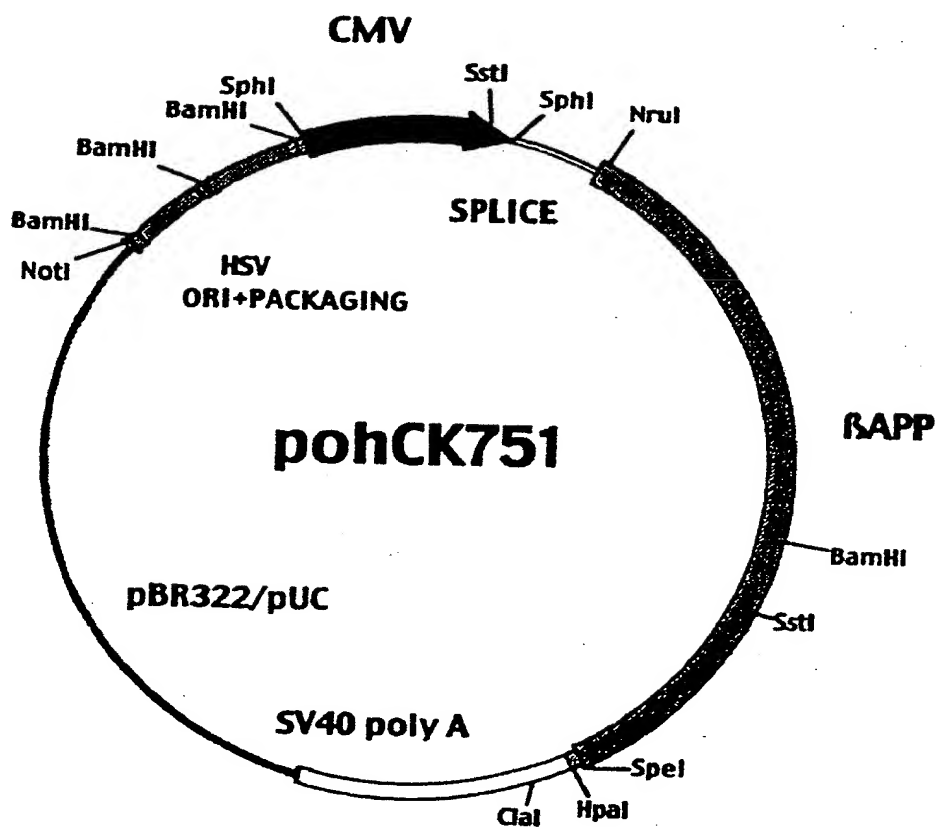


FIG. 21